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Pertussis Resurgence in Europe: Incidence and Epidemiologic Cycles in Immunization Required and Non-Required Countries

Sheryl Ann Duquet
Walden University

Walden University

College of Health Sciences

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Sheryl Ann Duquet

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Review Committee
Dr. Vibha Kumar, Committee Chairperson, Public Health Faculty
Dr. Richard Palmer, Committee Member, Public Health Faculty
Dr. Michael Furukawa, University Reviewer, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
2019

Abstract

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Immunization Required and Non-Required Countries

by

Sheryl Ann Duquet

MS, Wayne State University 1997

BS, University of Michigan 1993

Doctoral Study Submitted in Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Public Health

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2019

Abstract

Although pertussis vaccines have been available for over 7 decades, countries are experiencing a pertussis resurgence. This study sought to establish a relationship between the European pertussis immunization schedule designs (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required), which potentially influences immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis. The theoretical foundation for this study was the theory of herd immunity. A quantitative research method was used, supported by a secondary data source. The statistical analysis included the use of linear regression to evaluate the relationship between the requirement of the vaccine and the addition of adolescent boosters on the incidence level and the length of the epidemiologic cycles. The study findings suggest that pertussis immunization, whether recommended or required, does have an influence on the incidence rate within the populations of the countries analyzed. The same influence on incidence was demonstrated in relation to adolescent boosters as part of the immunization schedule. A similar relationship was *not* observed between the immunization schedule requirement and design on the epidemiologic cycles. This study provided relevant data that contributes to the enhanced understanding of the relationship between the design of the immunization schedule on incidence. This understanding could help control the resurgence, reduce immune waning through adolescent boosters, enhance immunization schedule timing, and lower the incidence. The result would be a positive public health social change through improved immunization strategy.

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Dedication

This doctoral study is dedicated to my husband, Matthew Jackson, for his endless support through the doctoral process. From the moment I decided to pursue my doctorate, he provided the encouragement that I needed to bring this educational journey to completion. I would also like to include in the dedication, my Grandmother Orena Koch, whom I lost before I could complete my doctoral degree. Her spirt has been with me throughout the final years of the doctoral process. Lastly, to Emma Duquet and Oliver Duquet for their continuous supply of love and joy.

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Section 1: Foundation of the Study and Literature Review

Introduction

Pertussis is the result of a human-acquired infection by the bacterium *Bordetella pertussis* and to a much lesser extent *Bordetella parapertussis,* transmitted via airborne droplets generated from a cough or a sneeze (Bouchez & Guiso, 2015). *B. pertussis* colonizes in the respiratory tract and the toxins contribute to the pathogenesis of the disease (Carbonetti, 2016). Pertussis has a 3-week incubation period prior to the first of three phases of the disease: catarrhal, paroxysmal, and convalescent phase, each lasting 1–2 weeks (Locht, 2016). The catarrhal stage involves nondescript symptoms such as a sore throat, dry cough, runny nose, and in less than 20% of infected individuals, a fever. The spasmodic stage is characterized by a paroxysmal cough, episodes of cyanosis from coughing and vomiting. The convalescent stage is the final stage of the disease, which brings a reduction in the severity of the cough and other related symptoms (Calvert & Heath, 2017). There are also several secondary complications associated with pertussis, which can prove fatal in infants, such as pneumonia, apnea, leukocytosis, and pulmonary hypertension (Carbonetti, 2016).

In the early 1900s, before the development of pertussis vaccines, it was understood that pertussis was not just a disease affecting children but a disease that was also found in adults, albeit in a much milder and less acute form (Clark, 2014). Following the development and use of whole-cell pertussis vaccines, the incidence of the disease was significantly reduced. However, it was understood that the pertussis vaccines did not provide lifelong immunity (Clark, 2014). Pertussis generally occurs in episodic cycles of 3–5 years, providing evidence that although the incidence of pertussis can be reduced, the transmission of the disease can continue throughout the population (Clark, 2014).

The purpose of vaccination for diseases like pertussis is to reduce the severity and mortality associated with the disease (World Health Organization [WHO], 2016). The causative agent of pertussis, *B. pertussis,* was determined in 1906. The bacterium, *B. pertussis,* was utilized to create the first vaccine against pertussis. The vaccine created was a whole-cell vaccine (Saadatian-Elahi et al., 2016). In 1940, clinical trial data became available, which supported the effectiveness of the whole-cell vaccine against pertussis (Clark, 2014). Pertussis whole-cell vaccines have been recommended for use in developed countries since the 1940s. This vaccine was eventually used globally until the 1990s when an acellular vaccine was developed with a safer safety profile. The acellular vaccine was adopted in many of the developed countries around the globe. However, most developing countries continue to utilize the whole-cell pertussis vaccine for economic reasons (Esposito & Principi, 2016). It is estimated that approximately 70% of the countries around the globe still utilize whole-cell pertussis vaccines (Bouchez & Guiso, 2015).

After the transition in some developed countries to the acellular pertussis vaccines, it was discovered that the immune response to the vaccine was not as long lasting as the pertussis whole-cell vaccine (Guiso et al., 2017). Although acellular pertussis vaccines do not produce the undesired side effects that the pertussis whole-cell vaccines do, they are not as effective in sustaining immunity as the whole-cell vaccines (Guiso et al., 2017). The lack of immune efficacy is likely due to the difference in how immunity is established in the body (Guiso et al., 2017). The pertussis acellular vaccine induces an immune response, which involves T helper 2 response without the involvement of T memory cells. The pertussis whole-cell vaccine activates T helper 1 and 17 response with the involvement of B and T memory cells. The immunologic pathway of the whole-cell vaccine provides longer lasting immunity (Guiso et al., 2017).

Because pertussis was long viewed as a disease of only infants and preadolescent children, immunization schedule recommendations for both acellular and whole-cell vaccines were structured to administer the primary series in Year 1 of life, followed by two boosters in Year 2 and Year 3/4 (Esposito & Principi, 2016). While whole-cell vaccines were in use, boosters were not administered to adolescents and adults because the side effects of the vaccine were more severe in older individuals. The introduction of acellular vaccines allowed for the introduction of boosters beyond the primary vaccination series provided in infants and young children (Bouchez & Guiso, 2015).

The structure of the immunization schedules provided a significant reduction in pertussis until a gradual increase of pertussis incidence was observed in the 1980s in areas with high pertussis vaccination rates (Esposito & Principi, 2016). Additionally, the incidence of pertussis diagnosed in adolescents and adults was increasing. In an attempt to reduce the pertussis incidence, recommendations for adolescent and adult boosters were also added to the immunization schedules in many countries (Esposito & Principi, 2016).

Pertussis is a disease that remains prevalent globally despite the fact that vaccines have been available since the 1940s (Locht, 2016). In some developed areas of the globe, where the pertussis vaccines have been in use for decades, such as the United States, United Kingdom, and Australia, a resurgence of pertussis has occurred (Sealy, Belcher, & Preston, 2016). Multiple significant outbreaks have occurred. These outbreaks have yielded different epidemiology compared to prior years. The main epidemiological difference is the age of the individuals contracting pertussis. Since the 1990s, while still considerably high in infants, the adolescent incidence of pertussis has been increasing (Sealy, Belcher, & Preston, 2016).

The resurgence of pertussis is a phenomenon that is occurring in both developed and developing countries throughout the world (Chen & He, 2017). The resurgence has estimated rates of infection for developed countries by up to 12% and up to 50% in developing countries. The incidence rate for this vaccine-preventable disease is most significant in children under the age of 2, with fatality rates of 0.2% in developed countries and 4% in developing countries (Chen & He, 2017). Both developed and developing countries have observed an epidemiological shift in an increase of pertussis in adolescents and adults (Chen & He, 2017).

Adolescents and adults are believed to be the primary source of infection transmission to children under the age of 2 years. Recognition of the epidemiological shift in an increase of pertussis in adolescents and adults is significant. because adolescents and adults have been found to be the primary source of infection of unprotected infants (Terranella et al., 2016). This is because of the epidemiological shift in the increase of pertussis in adolescents and adults, and the immune waning associated with the implementation of acellular pertussis vaccines, the understanding of the potential of the relationship between the design and requirement of pertussis immunization schedules on pertussis incidence and the associated epidemiologic cycles could assist in controlling the pertussis resurgence, reducing immune waning, enhancing immunization schedules, and lowering the incidence of pertussis, thus resulting in positive public health social change through improved immunization strategy.

Problem Statement

Despite the availability of pertussis vaccines for over 70 years, countries are experiencing a resurgence of pertussis among their populations (Della-Torre, Benevides, Pereira de Melo, & Ferreira, 2015). Globally, the annual estimate of the incidence of pertussis is up to 40 million cases; these are associated with approximately 300,000 deaths (Muloiwa, Kagina, Engel, & Hussy, 2015). The actual worldwide incidence of pertussis has not been accurately determined because of the variability in the reporting and collection of the epidemiology. The variability in the collection of the data has a significant effect on the understanding of the true incidence of pertussis (Esposito & Principi, 2016).

Another significant aspect associated with pertussis that has not been determined is a complete understanding of the disease pathogenesis.

Additionally, although the pertussis vaccines, both acellular and whole-cell, have been effective in reducing the incidence of pertussis, the immunological mechanisms of *B. pertussis* are not well understood (Lapidot & Gill, 2016). The use of the acellular pertussis vaccine has been linked to the resurgence of pertussis in developed countries due to evidence of immune waning. In addition to immune waning, there has also been an upsurge in the number of asymptomatic infections in adolescents, thus leading to increased transmission of the disease (Sealy, Belcher, & Preston, 2016). Pertussis is pervasive throughout the world; the true magnitude of its pervasiveness is unknown and is complicated due to the fact that asymptomatic pertussis infection is common in adolescents and adults (Sealy, Belcher, & Preston, 2016).

Older children, adolescents, and adults can also develop the disease, but the illness is not as severe as it is in infants, pregnant women, and the elderly, who are at higher risk for contracting pertussis (Guiso, 2014). An age incidence trend has also emerged as part of the resurgence of pertussis. The incidence involving adolescents in the age range of 13–16 has surfaced as a change in the historical trending of the disease. Infants, mainly those less than 3 months old, have the highest rate of pertussis-related deaths (Centers for Disease Control and Prevention [CDC], 2017). The increase in the incidence of detected and undetected pertussis in the adolescent and adult populations, along with immune waning, is believed to play a significant role in the continuation of the reservoir of circulating pertussis, and thus in the resurgence of pertussis in countries with well-established vaccination rates (Esposito & Principi, 2016).

A review of the literature on pertussis resurgence reveals gaps in understanding the cause and contributing factors associated with the resurgence. The literature does suggest some potential causes for the resurgence of pertussis, such as changes in the vaccine, bacterial genetic variations in the bacterium, immunity waning, and pertussis vaccine effectiveness (Althouse & Scarpino, 2015). Two additional proposed causes for the pertussis resurgence are the timing of initial and booster vaccination schedules (Riolo & Rohani, 2015) and the asymptomatic transmission of the disease caused by inadequate booster immunization coverage (Althouse & Scarpino, 2015).

The use of vaccines is an essential tool to protect public health against pertussis. Not only do vaccines protect the immunized individual, but they also create a state of herd immunity that protects the population (Sabbe & Vandermeulen, 2016). Pertussis vaccines have played a protective role in reducing the incidence of pertussis. However, with the implementation of acellular vaccines, immunity is waning at a more rapid rate than with whole-cell vaccines (Sabbe & Vandermeulen, 2016). There is also a significant variation in pertussis primary vaccination schedules globally. The type of vaccine utilized for the primary series, including the mixing of vaccine types during the series, also varies globally (WHO, 2016). A gap identified in the literature, and the focus of this study, is the understanding of the potential relationship between the type of acellular pertussis vaccine in use and the pertussis vaccination schedule, whether recommended or mandatory, has as contributing factors to the country's pertussis incidence and epidemiologic cycles. Additionally, the impact that a country's requirement for pertussis immunization, whether recommended or required, is also a gap in the literature.

Data collected via surveillance and statistical modeling provide evidence that the continued use of acellular pertussis vaccines will lead to an increased pertussis resurgence. The resurgence increases because, as immunity wanes following immunization, the risk of fatality to the unimmunized children who may contract the disease increases (WHO, 2016). The extent, severity, and timing of the resurgence are not known. The factors that play a potential role in the resurgence of pertussis, such as vaccine type, the structure of the vaccine schedule, and the vaccine coverage, need to be evaluated to lower the incidence of pertussis and stop the resurgence of the disease (WHO, 2016).

Purpose of the Study

This doctoral study was to establish if there was any relationship between the pertussis immunization schedule design (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required), which potentially influences immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis within a country's population. Multiple European countries with recommended and mandatory pertussis immunization schedules were included in the study. Immunity waning is suggested to be a contributing factor in the increase in pertussis incidence in both economically developed and developing countries (Sealy, Belcher, & Preston, 2016). This study provided evidence of the potential relationships associated with immunization schedule design and the immunization requirement on the incidence and frequency of epidemiologic cycles. The study findings related to immunization schedule design and the immunization requirement could also be utilized by health professionals to address the health and medical needs of populations that are at an elevated risk of contracting pertussis.

Research Questions and Hypotheses

This study was guided by the following four e research questions:

1. RQ1: Is there any association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis? The null hypothesis (H_0) is that there is not an association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis. The alternative hypothesis (H_1) is that there is an association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis.
2. RQ2: Is there any association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis? The null hypothesis (H_0) is that there is not an association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis. The alternative hypothesis (H_1) is that there is an association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis.

3. RQ3: Is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and incidence level of pertussis? The null hypothesis (H_0) is that there is not an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the incidence level of pertussis. The alternative hypothesis (H_1) is that there is an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the incidence level of pertussis.
4. RQ4: Is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles? The null hypothesis (H_0) is that there is not an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles. The alternative hypothesis (H_1) is that there is an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles.

Theoretical Foundation for the Study

The theoretical foundation for this doctoral study was the theory of *herd immunity,* that is, the indirect protection received by individuals who are susceptible to a given disease from those individuals in the population who are immune to the same given disease (Plans-Rubio, 2014). The theory of herd immunity suggests that infectious diseases that are contracted person-to-person are limited when a critical proportion of the population or the herd immunity threshold is protected through vaccination or natural immunity to the infectious disease, thus reducing the potential prevalence or resurgence of the disease in the population (Plans-Rubio, 2014). The reduction in the incidence of infectious disease is termed the *herd effect* (Holland & Chase, 2014). If herd immunity in a population does not meet the required threshold, the herd effect will still provide a protective buffer of the population against the infectious disease (Holland & Chase, 2014).

The pertussis vaccine aids in protecting individuals who are immunized from contracting pertussis (Domenech de Cellès, Riolo, Magpantay, Rohani, & King, 2014). However, research related to the transmission effects of pertussis is lacking and needs to be better defined. The incidence rates in populations that have high pertussis vaccination rates suggest that there is a herd immunity effect (Domenech de Cellès et al., 2014). Additionally, in populations with high pertussis vaccination rates, there is data to suggest that reduced transmission, shorter epidemiologic cycles, and reduction in the incidence of pertussis in unvaccinated infants strengthens the existence of herd immunity in the population (Domenech de Cellès et al., 2014).

The primary objective of pertussis immunization programs is the reduction of disease and the associated mortality, and the potential establishment of population herd immunity (Nitsch-Osuch et al., 2013). Vaccination schedules for pertussis vary significantly among the countries of the world (Nitsch-Osuch et al., 2013). Adherence to vaccination schedules and the use of appropriately timed boosters, when immunity against pertussis waning is suspected, are essential to the establishment of herd immunity (Nitsch-Osuch et al., 2013). Data from research studies have provided evidence that European countries need to incorporate booster vaccinations into their immunization schedules to strengthen individual and population protection, and the establishment of strong herd immunity against pertussis infection and transmission (Nitsch-Osuch et al., 2013). This study utilized four research questions to understand if there was any relationship between the pertussis immunization schedule design and the immunization requirement, which potentially influences immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis within a country's population. The dependent and independent variables linked with the research questions also helped establish if the vaccination schedule design, immunization requirement, and use of booster vaccinations provided evidence of a population herd immunity effect based on pertussis incidence.

Nature of the Study

This study utilized a quantitative research method, supported by a secondary data source, to help address the research questions. The quantitative research approach was used to evaluate the potential relationship between the requirement of the pertussis vaccine (recommended or required), and the addition of recommended or required adolescent boosters, on the incidence level and the length of the epidemiologic cycles of pertussis. The quantitative approach used aspects of descriptive analysis, measures of central tendency, and correlation coefficients for the statistical analysis. Additionally, the statistical analysis included measures of dispersion and inferential statistics.

The dependent variable for RQ1 was the pertussis incidence within the country's population. The independent variable for RQ1 was the pertussis vaccine schedule required by the country. The dependent variable for RQ2 was the pertussis epidemiologic cycles of pertussis within the country's population. The independent variable for RQ2 was the pertussis vaccine schedule required by the country. The dependent variable for RQ3 was the pertussis incidence level of pertussis within the country's population. The independent variable for RQ3 was the country's addition of required adolescent boosters to the pertussis vaccine schedule recommended by the country. The dependent variable for RQ4 was the length of the epidemiologic cycles of pertussis within the country's population. The independent variable for RQ4 was the country's addition of recommended adolescent boosters to the pertussis vaccine schedule required by the country.

Literature Review Search Strategy

The literature review was carried out with the following databases: PubMed, Science Direct, CINAHL, Medline, and Google Scholar. The following search terms were used: *pertussis*, *vaccines*, resurgence*, schedules, boosters, asymptomatic, incidence,* and *epidemiologic cycles*. The review was limited to a 5-year timeframe, and focused on information gathered from peer-reviewed journals.

Literature Review and Related Key Variables and/or Concepts

Pertussis is a vaccine-preventable disease, but the incidence of the disease continues to rebound in countries with high vaccination rates (Esposito & Principi, 2016). The expert panel assembled for the 2015 Pertussis: Biology, Epidemiology, and Prevention Conference determined that improving current vaccine strategies, as well as the creation of more effective vaccines would be required to address the ongoing challenges with the global control of pertussis. The panel of experts determined that there are multiple factors associated with the continued elevated incidence, and in some countries, the resurgence of pertussis despite adequate vaccination programs. The factors identified were vaccine strategy, population composition, surveillance systems, and methods of detection (Saadatian-Elahi et al., 2016).

Tan et al. (2015) examined the pertussis incidence trends from a global aspect and determined that underreporting of pertussis is a significant problem. Under-reporting of pertussis is most prevalent in adult and adolescent populations. Global under-reporting of pertussis appears to be in part associated with several factors, such as the type of surveillance system, the robustness of the surveillance system, health system infrastructure, and healthcare technological capabilities (Tan et al., 2015). The adolescent and adult populations are the most challenging to detect pertussis incidence due to the generalized characteristics and the lessened severity of pertussis in the adolescent and adult populations. In the adolescent and adult populations, pertussis presents as a persistent, but not severe cough, unlike the severe illness experienced by young children and infants (Tan et al., 2015).

European countries have experienced a resurgence of pertussis, as the other regions around the globe have, despite having established immunization programs and surveillance systems in place (Heiniger et al., 2016). Due to the multifaceted aspects of the disease dynamics associated with pertussis, the cause of the resurgence of pertussis in Europe and other regions of the world has not been established. However, it has been determined that the transmission of pertussis by adolescents and adults with waning pertussis immunity has caused the continuation of pertussis epidemiologic cycles in European countries (Heiniger et al., 2016).

There are two important aspects of the available pertussis vaccines, which is protection from disease and infection (Locht, 2016). Recommendations based on current research suggest that countries who have not yet switched to the acellular vaccine do not make the switch to aid in better protection against infection and to increase disease control. It has also been recommended that until more effective pertussis vaccines are developed, the optimal use of current vaccines is needed to control infection and prevent disease (Locht, 2016).

Gambhir et al. (2015) utilized epidemiological modeling to examine the recent pertussis upsurge in the United States. The modeling identified variations in the pertussis efficacy and immune protection duration. The study compared whole-cell and acellular vaccines. The study results indicated the need to perform more extensive modeling to examine alternative pertussis vaccination schedules, to aid in addressing the resurgence. The alternate vaccination schedules would include adjustments to the age of vaccination, the age of booster doses, and cocooning strategies (Gambhir, Clark, Cauchemez, Tartof, Swerdlow, & Ferguson, 2015).

Choi, Campbell, Amirthalingam, Jan van Hoek, and Miller (2016) developed a mathematical model to examine the transmission of pertussis to gain an understanding of the revival of pertussis in the countries of England and Wales. The model also examined the potential effect of the introduction of the addition of a different vaccination schedule. The modeling presented data that indicated that countries currently using a pertussis whole-cell vaccine should not transition to an acellular vaccine unless enhanced vaccination strategies are developed. Additionally, the modeling indicated that a more effective pertussis vaccine is needed to lessen the resurgence (Choi, Campbell, Amirthalingam, Jan van Hoek, & Miller, 2016).

Believing that the change from a whole-cell to an acellular vaccine has influenced the pertussis resurgence in the country of New Zealand, Radke, Petousis-Harris, Watson, Gentles, and Turner (2016) examined the effectiveness of the acellular vaccine schedule utilized in New Zealand. The authors found that the vaccine protection from the immunization schedule only provides protection through age four. The study concluded that introducing a pertussis vaccine booster at age six would enhance childhood immunity (Radke, Petousis-Harris, Watson, Gentles, & Turner, 2016).

Definitions

Adolescent Booster: Supplemental doses of a vaccine intended to boost the immunity of an adolescent (U.S. Health and Human Services, 2018).

Asymptomatic Infection: Infection occurring with apparent symptoms (U.S. Health and Human Services, 2018).

Epidemiologic Cycle: The length of time between the increase of pertussis incidence over time in a given population (Domenech de Celles, Magpantay, King, & Rohani, 2016).

Herd Immunity: The indirect protection received by individuals who are susceptible to a given disease from those individuals in the population who have immunity to the same given disease (Plans-Rubio, 2014).

Immunization Schedule: Is a schedule of immunization requirements based on age, number of doses, and timing of the doses of a vaccine (Kim, D, Bridges, & Harriman, 2015).

Pertussis Incidence: The quantity of new pertussis cases reported associated with a population during a defined period (U.S. Health and Human Services, 2018).

Pertussis Resurgence: The increase in the incidence of reported pertussis cases (Kilgore, Salin, Zervos, & Schmitt, 2016).

Pertussis Acellular Vaccine: A vaccine made from purified components of inactivated bacteria *Bordetella pertussis* (Kilgore, Salin, Zervos, & Schmitt, 2016).

Pertussis Whole-Cell Vaccine: A vaccine made from a suspension of whole inactivated *Bordetella pertussis* bacteria (Kilgore, Salin, Zervos, & Schmitt, 2016).

Recommended Immunization: Vaccines that are recommended, but not required by law for specific populations as part of the national immunization program of a given country (Haverkate et al., 2012).

Required Immunization: Vaccines that are required by law for specific populations as part of the national immunization program of a given country (Haverkate et al., 2012).

Waning Immunity: The reduction or loss of immune protecting antibodies over a period of time (U.S. Health and Human Services, 2018).

Assumptions

The data associated with the data set utilized for this study were presumed to be accurate. The database contained data from 1980 to 2017 and was updated annually. The database utilized for the study was the most up-to-date available.

Scope and Delimitations

The WHO database, Vaccine-Preventable Disease: Monitoring System 2018 Global Summary (WVPDMSGS), contains global vaccination data. European countries utilizing acellular pertussis vaccines with recommended and required immunization schedules were chosen for the study. Understanding any identified differences in pertussis incidence and epidemiologic cycles potentially associated with immunization schedules helped develop an awareness of the potential need for the adjustment of immunization schedule strategies to strengthen waning immunity.

Social Significance

This study was expected to provide data to help explain the factors that may be contributing to the resurgence and persistence of pertussis; the data generated from this doctoral study was expected to provide an enhanced understanding of the relationship between the design and requirement of the immunization schedule on pertussis incidence and epidemiologic cycles. Understanding the potential of this relationship could assist in controlling the pertussis resurgence, reduce immune waning, enhance immunization schedules, and lower the incidence of pertussis resulting in positive social change through improved immunization strategy. Specifically, the study outcomes could be applied in the field of public health through improvements in immunization schedules and strategies to be used in vaccination programs, and then appropriately applied within economically developed and developing countries.

Summary

Pertussis vaccines have been available for more than 70 years, but countries around the globe are experiencing a resurgence of pertussis among their populations (Della-Torre, Benevides, Pereira de Melo, & Ferreira, 2015). The global annual estimate of the incidence of pertussis is more than 40 million cases; these are associated with approximately 300,000 deaths (Muloiwa, Kagina, Engel, & Hussy, 2015). The true worldwide incidence of global pertussis has not been determined because of the significant variability in the reporting and collection of epidemiologic data (Esposito & Principi, 2016).

Following the development and use of whole-cell pertussis vaccines, the incidence of pertussis was significantly reduced. However, it was understood that these vaccines did not provide lifelong immunity (Clark, 2014). Pertussis generally occurs in cycles of 3 to 5 years, providing evidence that although the incidence of pertussis can be reduced, the transmission of the disease can continue throughout the population (Clark, 2014).

A gap identified in the literature was the understanding of the potential relationship between the type (acellular or whole-cell) of pertussis vaccine in use, and whether the pertussis vaccination schedule has contributing factors to the country's pertussis incidence and epidemiologic cycle. An additional gap in the literature associated with pertussis was the impact of a country's pertussis vaccination requirement, whether recommended or required, on the country's pertussis incidence and epidemiologic cycles. Therefore, the aim of this study was to establish whether there is any relationship between the pertussis immunization schedule design (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required), which could influence immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis within the country's population.

Multiple European countries with recommended and mandatory pertussis immunization schedules were included in the study. The study used a quantitative research method, supported by a secondary data source, to help address the research questions. A quantitative research approach was used to evaluate the potential relationship between the requirement of the pertussis vaccine (recommended or required) and the addition of recommended or required adolescent boosters on the incidence level and the length of the epidemiologic cycles of pertussis. This doctoral study provided data to help explain the factors that may be contributing to the resurgence and persistence of pertussis. Additionally, the data generated from this doctoral study provided an enhanced understanding of the relationship between the design and requirement of the immunization schedule on pertussis incidence and epidemiologic cycles.

Section 2: Research Design and Data Collection

Introduction

The purpose of this section is to describe and outline the research design and method of data collection. The research design examines the potential association between the pertussis immunization schedule design (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required). The association of the vaccine schedule and immunization requirement potentially influence immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis within the country's population. Multiple European countries with recommended and mandatory pertussis immunization schedules are included in the study.

Research Design and Rationale

The secondary data source that was utilized in this study was the WVPDMSGS. The selected database was developed by the WHO. The database offers global pertussis data associated with population data, reported cases, vaccination rates, immunization schedules, and immunization indicators (WHO, 2017). The data associated with the recommendation or requirement of pertussis immunization schedules was collected from the European Centre for Disease Prevention and Control Vaccine Scheduler (European Centre for Disease Prevention and Control, 2018).

The WVPDMSGS was selected because it provides the population information required to answer the research questions at the country level. The European countries chosen to be assessed in the doctoral study were based on their requirement for pertussis immunization vaccine used within the country and the inclusion of adolescent boosters in the vaccine schedule. All of the European countries chosen used acellular pertussis vaccines.

The WVPDMSGS database was used to examine this study's four research questions. Each of the four research questions involved the examination of the required (mandatory by law) immunization schedule or the recommended (voluntary) immunization schedule of the European countries involved in the study. The dependent variable for RQ1 was the pertussis incidence within the country's population. The independent variable for RQ1 was the pertussis vaccine schedule required by the country. The dependent variable for RQ2 was the pertussis epidemiologic cycles of pertussis within the country's population. The independent variable for RQ2 was the pertussis vaccine schedule required by the country. The dependent variable for RQ3 was the pertussis incidence level of pertussis within the country's population. The independent variable for RQ3 was the country's addition of required adolescent boosters to the pertussis vaccine schedule recommended by the country. The dependent variable for RQ4 was the length of the epidemiologic cycles of pertussis within the country's population. The independent variable for RQ4 was the country's addition of recommended adolescent boosters to the pertussis vaccine schedule required by the country.

Methodology

Population

The population consisted of European countries utilizing pertussis acellular vaccines. The countries were selected based on their recommendations or required pertussis immunization schedules. Additionally, countries recommending and requiring adolescent pertussis vaccines were included.

Sampling Procedure

Secondary data from the WVPDMSGS database was used for this doctoral study. The WVPDMSGS database contains immunization data that is assembled and assessed on an annual basis. The WHO works in partnership with the United Nations Children's Fund (UNICEF) to collect the data that populates the WVPDMSGS database (WHO, 2011).

The primary source of the data for the database is collected using joint reporting forms that were created in collaboration with WHO, UNICEF, and the ministries of health from participating member states. The forms were created to collect information associated with the participating countries' immunization coverage, reported vaccine-preventable diseases, immunization schedules, and immunization system performance indicators (WHO, 2011). Additional data included in the database is collected from the published literature that is evaluated by WHO, UNICEF, and experts from the locations referenced in the literature, UNICEF historical databases, and surveys provided by participating ministries of health (WHO, 2011).

The data were sampled based on the date range and countries selected to be evaluated as part of the doctoral study. A power analysis was performed to determine the sample size required to assure statistical significance. The data was not be altered from the reported values. IRB approval through Walden University to utilize the secondary data was obtained prior to evaluating the data (12-24-18-0543758).

Instrumentation and Operationalization of Constructs

This doctoral study used secondary data from a public database. The database used was the WVPDMSGS database. The database data was collected and verified by WHO, UNICEF, and select ministries of health and is updated on a yearly basis. The process of establishing the validity and reliability of the data used to populate the database was performed by WHO, UNICEF, local experts, and external reviewers.

The WVPDMSGS database was established in 2010 following a retrospective review by WHO and UNICEF of immunization data starting in the year 2000. The data being evaluated extended back to 1980 (WHO, 2011). The 2010 database was created to establish an accurate estimate of the immunization coverage of a variety of vaccine-preventable diseases (Burton et al., 2009). Since 2010, the database has been updated on an annual basis (WHO, 2011). WHO and UNICEF collaborate with the individual countries, working closely with them to understand and improve the accuracy and quality of the data (Burton et al., 2009).

The data collected for the database came from four primary sources, official immunization data reported from WHO member states, UNICEF historic immunization database, published literature, and surveys from ministries of health (WHO, 2011). The data were evaluated for a true reflection of immunization performance and potentially compromised data, as well as for potential biases, factualness of the information, and to verify that the data was obtained from reliable sources (WHO, 2011). The method used to evaluate and compile the data involves eight principles, which are: using evidence-based data, country-specific data, consistent patterns and trends, local expertise, no averaging of data, no smoothing of data, no 100% coverage of data, and determining the proportion of live births utilizing a mathematical model (WHO, 2011).

The process of data evaluation was conducted in multiple steps. The data is first collected and then was reviewed by WHO and UNICEF to check for accuracy against the reported national data, assessing if the data is compromised or inaccurate in regards to immunization coverage (WHO, 2011). Discrepancies are handled by contacting the reporting country to investigate discrepancies. Whenever possible, WHO and UNICEF work with experts from the reporting countries. Based on the official data reviewed and evaluated, draft estimates of immunization coverage are calculated (WHO, 2011).

The next step in the data evaluation process was to have the data reviewed by national authorities. The national authorities review the data for accuracy based on local knowledge and expertise. Following the national authority review, the draft estimates are revised by the WHO and UNICEF (WHO, 2011). The last step in the data evaluation process was to have the data undergo an external review by immunization experts with specialized expertise in immunization systems and methodology associated with surveys. Any additional revisions, as an outcome of the external review, are performed by WHO and UNICEF, and the data was then added to the database and disseminated for public access (WHO, 2011).

The operationalization of the variables collected for the doctoral study is outlined in Table 1. The variable data was obtained from the WVPDMSGS database. The nominal variables are immunization schedule recommended, immunization schedule required, adolescent boosters recommended, and adolescent boosters required. The categorical variables are pertussis incidence and length of the epidemiologic cycle.

Table 1

Operationalization of Variables Collected from WHO Vaccine-Preventable Disease: Monitoring System 2018 Global Summary database

Variable	Values	Research Question
Pertussis incidence	Value	RQ 1, 3
Immunization schedule required	Yes/No	RQ 1, 2
Length of epidemiologic cycle	Value	RQ 2, 4
Adolescent boosters required	Yes/No	RQ 3, 4

Data Analysis Plan

The intention of the doctoral study was to establish if there was any relationship between the pertussis immunization schedule design (with versus without the inclusion of adolescent boosters) and the immunization requirement (recommended versus required), which potentially influences immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis within the country's population. Data from this study were analyzed using SPSS version 24. SPSS version 24 was used to screen and clean the data before the data is used in the analysis of the research questions. The data were assessed for any missing variables, outliers, skewness, and to assure that the variables meet the statistical assumptions that are associated with the statistical analysis that will be performed as part of the doctoral study.

The data analyzed from the WVPDMSGS database focused on European countries utilizing acellular pertussis vaccines. The quantitative research approach was used to evaluate the potential relationship between the requirement of the pertussis vaccine (recommended versus required) and the addition of recommended versus required adolescent boosters on the incidence level and the length of the epidemiologic cycles of pertussis. The quantitative approach used aspects of descriptive analysis, measures of central tendency, and correlation coefficients for the statistical analysis. The qualitative approach also included a determination of the P-value, confidence intervals, mean, standard deviation, and F-test as specific tests of statistical significance. Additionally, the statistical analysis included linear regression to evaluate the potential relationship between the requirement of the pertussis vaccine (recommended versus required) and the addition of recommended versus required adolescent boosters on the incidence level and the length of the epidemiologic cycles of pertussis for each of the respective research questions that have been broken out into four independent questions.

In order to understand the relationship amid the dependent variable and the independent variable associated with the research question, linear regression analysis was used to evaluate the research question. The linear regression analysis aided in predicting the value of the dependent variable based on the independent variable in order to understand the nature of the relationship between the variables. The linear regression analysis also assisted in understanding how dependent variable changes in conjunction with changes in the independent variable associated with the research question. The results of the linear regression analysis were interpreted by examining the correlation and direction of the research data, evaluating the best fitting line, and assessing the strength of the relationship between the variables. Specifically, the data analysis will involve determining and assessing the linear regression equation, the coefficient of the multiple determination (R^2), the significance level, and the confidence intervals. This statistical approach was applied to all four research questions.

Due to undiscernible differences in the outcome of the linear regression as it relates to the independent variables from the research questions analyzed via linear regression, ANOVA was utilized to determine if there is a significant difference between the independent variables. The ANOVA allowed for a potential determination of the variance between the variables by comparing the means of the independent variables. Specifically, the descriptive statistics, such as the mean, standard deviation, standard error, and confidence intervals were evaluated. Additionally, the Sum of Squares, Mean Square, and significance levels were determined to aid in the analysis. This additional statistical approach was applied to all four research questions.

RQ1: Is there any association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis? The null hypothesis (H_0) is that there is not an association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis. The alternative hypothesis (H_1) is that there is an association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis. The dependent variable for RQ1 is the pertussis incidence (number of reported cases) within the country's population. The independent variable for RQ1 is the pertussis vaccine schedule required by the country (Yes/No). The research question was analyzed with linear regression to determine a potential relationship between the independent and dependent variables. The statistical analysis included a determination of the P-value, confidence intervals, mean, standard deviation, and F-test as specific tests of statistical significance. ANOVA was applied to determine if there was a difference between the independent variables from the research questions analyzed via Linear regression.

RQ2: Is there any association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis? The null hypothesis (H_0) is that there is not an association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis. The alternative hypothesis (H_1) is that there is an association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis. The dependent variable for RQ2 is the pertussis epidemiologic cycles (length of time between spikes in incidence) of pertussis within the country's population. The independent variable for RQ2 is the pertussis vaccine schedule required by the country (Yes/No). The research question was analyzed with linear regression to determine a potential relationship between the independent and dependent variables. The statistical analysis included a determination of the P-value, confidence intervals, mean, standard deviation, and F-test as specific tests of statistical significance. ANOVA was applied to determine if there was a difference between the independent variables from the research questions analyzed via Linear regression.

RQ3-Quantitative: Is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and incidence level of pertussis. The null hypothesis (H_0) is that there is not an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the incidence level of pertussis. The alternative hypothesis (H_1) is that there is an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the incidence level of pertussis. The dependent variable for RQ3 is the pertussis incidence level of pertussis (number of reported cases) within the country's population. The independent variable for RQ3 is the country's addition of required adolescent boosters to the pertussis vaccine schedule recommended by the country (Yes/No). The research question was analyzed with linear regression to determine a potential relationship between the independent and dependent variables. The statistical analysis included a determination of the P-value, confidence intervals, mean, standard deviation, and F-test as specific tests of statistical significance. ANOVA was applied to determine if there was a difference between the independent variables from the research questions analyzed via Linear regression.

RQ4: Is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles. The null hypothesis (H_0) is that there is not an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles. The alternative hypothesis (H_1) is that there is an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles. The dependent variable for RQ4 is the length of the epidemiologic cycles (length of time between spikes in incidence) of pertussis within the country's population. The independent variable for RQ4 is the country's addition of recommended adolescent boosters to the pertussis vaccine schedule required by the country (Yes/No). The research question was analyzed with linear regression to determine a potential relationship between the independent and dependent variables. The statistical analysis included a determination of the P-value, confidence intervals, mean, standard deviation, and F-test as specific tests of statistical significance. ANOVA was applied to determine if there was a difference between the independent variables research questions analyzed via linear regression.

Threats to Validity

This doctoral study has potential threats to the internal and external validity of the data being used to assess the research questions. Some of the potential internal validity threats are associated with the data contained in the WVPDMSGS database. Although the data was evaluated for accuracy and reliability, the entry of the data into the database and the aggregation of the data from the various reporting sources can be a potential threat to validity if they are not performed per the WHO and UNICEF prescribed principles. Additionally, the validity of the data could also be compromised if adequate reviews of the data are not performed by the WHO, UNICEF, local experts, and external reviewers.

External validity threats also exist associated with the WVPDMSGS database. External threats to the validity of the data being used to assess the research questions are the accuracy of the reporting and calculation of the immunization coverage from the participating member states. Additionally, biases can be created if the participating member states fail to report portions of the population, or over or underestimate the vaccination coverage and incidence of the vaccine-preventable diseases.

Ethical Procedures

Walden University IRB approval was obtained to use the public WVPDMSGS secondary data for this doctoral study. The data contained in the WVPDMSGS does not include any data that is required to be de-identified. The data was handled in an ethical manner during the statistical evaluation. All of Walden University's ethical procedures were followed during the statistical analysis of the doctoral study data. Following the statistical analysis of the data in SPSS, and completion of the doctoral study, the data will be protectively stored in the SPSS format, along with a copy of the WVPDMSGS database for the prescribed period under Walden University policy.

Summary

The research design utilized in this doctoral study examined the potential association between the pertussis immunization schedule design (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required). The secondary data source that was used in the doctoral research study was the WVPDMSGS.

The study population consisted of European countries utilizing pertussis acellular vaccines. The countries were selected based on their recommendations or required pertussis immunization schedules. Additionally, countries recommending and requiring adolescent pertussis vaccines were included. The study hypotheses were evaluated via SPSS version 24 software. The four research questions explored were (a) is there any association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis, (b) is there any association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis, (c) is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and incidence level of pertussis, and (d) is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles.

A quantitative research approach was used to evaluate the potential relationship between the requirement of the pertussis vaccine (recommended or required) and the addition of recommended or required adolescent boosters on the incidence level and the length of the epidemiologic cycles of pertussis. The quantitative approach used aspects of descriptive analysis, measures of central tendency, and correlation coefficients for the statistical analysis. Additionally, the statistical analysis included measures of dispersion and inferential statistics.

Section 3: Presentation of Results and Findings

Introduction

The aim of this doctoral study was to establish whether there was any relationship between the pertussis immunization schedule design (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required), which potentially influences immunity waning, and thus the incidence rate and epidemiologic cycles of pertussis within the country's population. The dependent variables examined in the study were the pertussis incidence within a country's population and the pertussis epidemiologic cycles of pertussis within a country's population. The independent variables examined were the pertussis vaccine schedule recommended by the country, the pertussis vaccine schedule required by the country, the country's addition of recommended adolescent boosters to the pertussis vaccine schedule, and the addition of required adolescent boosters to the pertussis vaccine schedule required by the country. The research questions and associated hypotheses are presented below.

1. RQ1: Is there any association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis? $H_0 1$: There is not an association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis. $H_1 1$: There is an association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis.

2. RQ2: Is there any association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis?

$H_0$2: There is not an association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis.

$H_1$2: There is an association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis.

3. RQ3: Is there any association between the European country's addition of

$H_0$3: There is not an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the incidence level of pertussis.

$H_1$3: There is an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the incidence level of pertussis.

4. RQ4: Is there any association between the European country's addition of

$H_0$4: There is not an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles.

$H_1$4: There is an association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles.

This section outlines the presentation of the results and findings of the doctoral study. In addition to the introduction, which describes the aim of the doctoral study, research questions, and the associated hypotheses, the section provides a description of the data collection, and the secondary data set used to answer the doctoral study research questions. Additionally, the results obtained from the linear regression analysis are described and discussed for each of the research questions. Lastly, the data analysis findings and interpretations are summarized.

Data Collection of Secondary Dataset

Secondary data from the WVPDMSGS database was used to explore the research questions associated with this doctoral study. The WVPDMSGS database contains immunization data that is assembled and assessed on an annual basis. The WHO works in partnership with UNICEF to collect the data that populates the WHO Vaccine-Preventable Disease: Monitoring System Global Summary database (WHO, 2011).

The primary source of the data for the database is collected using joint reporting forms that were created in collaboration with WHO, UNICEF, and the ministries of health from participating member states. The forms were created to collect information associated with the participating country's immunization coverage, reported vaccine-preventable diseases, immunization schedules, and immunization system performance indicators (WHO, 2011). Additional data included in the database is collected from the published literature that is evaluated by WHO, UNICEF, and experts from the locations referenced in the literature, UNICEF historical databases, and surveys provided by participating ministries of health (WHO, 2011). The database data is collected and verified by WHO, UNICEF, and select ministries of health and is updated on a yearly basis. The process of establishing validity and reliability of the data used to populate the database is performed by WHO, UNICEF, local experts, and external reviewers.

The first stage in the evaluation of the secondary data from the WVPDMSGS database was to identify which European Union countries require pertussis immunization schedule, and which European Union countries have recommended pertussis immunization schedules. Additionally, which European Union countries required, or recommended adolescent pertussis booster needed to be determined. The European Centre for Disease Prevention and Control Vaccine Scheduler was utilized to determine the recommendation or requirement of pertussis immunization schedules and adolescent boosters. There was a total of 29 European Union countries identified that had a required or recommended pertussis immunization schedule. Nine of the European Union countries required pertussis immunization schedules and 20 had recommended pertussis immunization schedules.

The secondary data from the WVPDMSGS database was reviewed based on the identified European Union countries. The date range evaluated as part of the doctoral study was from 2010 to 2017, in order to stay within the last decade. The criteria set for missing data per country was no more than one data point could be missing. The criteria set for the population range was greater than one million people, but less than 11 million people. The countries that meet the established criteria were Austria, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Hungary, Ireland, Latvia, Lithuania, Norway, Portugal, Slovakia, Slovenia, and Sweden. Of the 15 countries that meet the missing data and population criteria, 7 had required pertussis immunization schedules, and 8 had recommended pertussis immunization schedules. The incidence data for each of the 15 selected European Union countries were normalized by dividing the incidence per 100,000 people.

The data for the epidemiologic cycles was evaluated by taking the average of the 8 years being evaluated for each of the 15 selected European Union countries and then determining the value above or below the baseline incidence per country. The data evaluation resulted in a data set containing 117 data points. The adolescent pertussis booster data was also evaluated. It was determined that of the seven countries that required pertussis immunization schedules, five of the seven required adolescent pertussis boosters. In regard to the eight European Union countries that recommended pertussis immunization schedules, six of the eight countries also had recommended adolescent pertussis boosters as part of the immunization schedule. The four European Union countries without a required or recommended adolescent European booster as part of the pertussis immunization schedule, were Denmark, Portugal, Croatia, and Latvia. The data evaluation resulted in a data set containing 86 data points.

Analysis

The doctoral study statistical analysis included the use of linear regression to evaluate the potential relationship between the requirement of the pertussis vaccine (recommended versus required) and the addition of recommended versus required adolescent boosters on the incidence level and the length of the epidemiologic cycles of pertussis for each of the respective research questions that have been broken out into four independent questions. Linear regression required an independent variable and one dependent variable to perform the analysis for each of the research questions.

In order to understand the potential relationship between the dependent variable and the independent variable associated with the research question, linear regression analysis was used to evaluate the research questions. The linear regression analysis aided in predicting the value of the dependent variable based on the independent variable in order to understand the nature of the relationship between the variables. The linear regression analysis also assisted in understanding how the dependent variable changed in conjunction with changes in the independent variable associated with the research questions. The outcome of the linear regression analysis was interpreted by examining the correlation and direction of the research data, evaluating the best fitting line, and assessing the strength of the relationship between the variables. The data analysis involved determining and assessing the linear regression equation, the coefficient of the multiple determination (R^2), the significance level, and the confidence intervals. This statistical approach was applied to all four research questions.

ANOVA was utilized to determine if there is a significant difference between the independent variables associated with the research questions. The ANOVA allowed for the potential determination of the variance between the variables by comparing the means of the independent variables. The descriptive statistics, such as the mean, standard deviation, standard error, and confidence intervals, were evaluated. Additionally, the Sum of Squares, Mean Square, and significance levels were determined to aid in the analysis. This statistical approach was applied to all four research questions.

Results

Research Question 1

The data associated with research question 1 was analyzed utilizing Linear regression. The research questions was:

> RQ 1: Is there any association between the pertussis vaccine schedule that is required by the European country and the incidence level of pertussis?

The linear combination of required and recommended immunization schedules was found to be significantly related to pertussis incidence in the European countries evaluated as part of the doctoral study. The $R^2 = .056$, $F(1,115) = 6.78$, $p = .010$. The Coefficient of Determination was .056, indicating that approximately 5.6% of the variance in the dependent variable pertussis incidence in the population can be accounted for by the linear relationship of the independent variable of required and recommended immunization schedules. The descriptive characteristics, linear regression model summary, ANOVA, and linear regression coefficients data are exhibited in Tables 2, 3, 4, and 5 below.

Table 2

Descriptive Characteristics of Vaccine Schedule Type and Incidence of Pertussis

Variable	N	Mean	Std Dev
Pertussis incidence	117	10.8651	17.49083
Required schedule	117	.4701	.50125
Recommended schedule	117	.5299	.50125

The mean of the pertussis incidence was 10.8651. The mean of the recommended schedule data was larger than the mean of the required schedule data by .0598.

Table 3

Linear Regression Associated with the Relationship of Vaccine Schedule Type and Incidence of Pertussis

Model	N	R	Square	Adjusted R Square	Standard Error of the Estimate
	117	.236	.056	.047	17.07051

Table 4

ANOVA Associated with the Relationship of Vaccine Schedule Type and Incidence of Pertussis

Model	Sum of Squares	df	Mean Squares	F	Sig
Regression	1976.503	1	1976.503	6.783	.010
Residual	33511.264	115	291.402		
Total	35487.768	116			

The F-Test, with a value of 6.783, indicates that the independent variables (required or recommended schedules) do have explanatory power over the dependent variable (pertussis incidence). The significance (P value) was .010, which is less than .05.

Table 5

Linear Regression Coefficient Associated with the Relationship of Vaccine Schedule Type and Incidence of Pertussis

Model	N	Coeff Std Error	t	sig	95% Conf Lower	95% Conf Upper
Required	117	3.162	2.604	.010	1.972	14.498

The value of t falls between the lower and upper confidence limits for both the recommended and required schedules. The t value was 2.604, with a 95% lower confidence limit of 1.972 and a 95% upper confidence limit of 14.498. The coefficients had a positive relationship. The effect size was .236 indicating a small level of relationship. The significance (P value) was .010, which is less than .05, thus rejecting the null hypothesis.

Research Question 2

The data associated with Research Question 2 were analyzed via linear regression. The research questions was:

> RQ2: Is there any association between the pertussis vaccine schedule that is required by the European country and the epidemiologic cycles of pertussis?

The linear combination of required and recommended immunization schedules was not significantly related to pertussis epidemiologic cycles in the European countries evaluated as part of the doctoral study. The $R^2 = .001$, $F(1,115) = .119$, $p = .731$. Coefficient of Determination was .001. Therefore, the required or recommended immunization schedules are not a good predictor of the pertussis epidemiologic cycles in the European countries evaluated as part of the doctoral study. The descriptive characteristics, linear regression model summary, ANOVA, and linear regression coefficients data are exhibited in Tables 6, 7, 8, and 9 below.

Table 6

Descriptive Characteristics of Vaccine Schedule Type and Epidemiologic Cycles of Pertussis

Variable	N	Mean	Std Dev
Pertussis cycle	117	.3335	10.33511
Required schedule	117	.4701	.50125
Recommended schedule	117	.5299	.50125

The mean of the pertussis cycle was .3335. The mean of the recommended schedule data was larger than the mean of the required schedule data by .0598.

Table 7

Linear Regression Associated with Vaccine Schedule Type and Epidemiologic Cycles of Pertussis

Model	N	R	R Square	Adjusted R Square	Standard Error of the Estimate
	117	.032	.001	- .008	10.37460

Table 8

ANOVA Associated with the Vaccine Schedule Type and the Epidemiologic Cycles of Pertussis

Model	Sum of Squares	df	Mean Squares	F	sig
Regression	12.771	1	12.503	.119	.731
Residual	12377.717	115	107.632		
Total	12390.488	116			

The F-Test, with a value of .119, indicates that the independent variables (required or recommended schedules) do not have explanatory power over the dependent variable (pertussis cycle). The significance (P value) was .731, which is greater than .05.

Table 9

Linear *Regression Associated with Vaccine Schedule Type and Epidemiologic Cycles of Pertussis*

Model	N	Coeff Std Error	t	sig	95% Conf Lower	95% Conf Upper
Required	117	1.922	.344	.731	-3.145	4.468

The value of t falls between the upper and lower confidence limits for both the recommended and required schedules. The t-value was .344, with a 95% lower confidence limit of -3.145 and a 95% upper confidence limit of 4.468. The coefficients had a positive relationship. The effect size was .032 indicating a small relationship. The significance (P value) was .731, which is greater than .05, thus not rejecting the null hypothesis.

Research Question 3

The data associated with Research Question 3 was analyzed utilizing Linear regression. The research questions was:

RQ3: Is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and incidence level of pertussis?

The linear combination of the addition of a required or recommended adolescent booster was significantly related to pertussis incidence in the European countries evaluated as part of the doctoral study. The $R^2 = .063$, $F(1,84) = 5.680$, $p = .019$. The coefficient of determination was .063, indicating that approximately 6.3% of the variance of the dependent variable pertussis incidence in the population can be accounted for by the linear combination of the independent variable of required and recommended adolescent boosters. The descriptive characteristics, linear regression model summary, ANOVA, and linear regression coefficients data are exhibited in Tables 10, 11, 12, and 13 below.

Table 10

Descriptive Characteristics Associated with Adolescent Booster Schedule Type and Incidence of Pertussis

Variable	N	Mean	Std Dev
Pertussis incidence	86	12.4801	19.60548
Required schedule	86	.470	.502
Recommended schedule	86	.530	.502

The mean of the pertussis incidence was 12.4801. The mean of the recommended schedule data was larger than the mean of the required schedule data by .060.

Table 11

Linear Regression Associated with Adolescent Booster Schedule Type and Incidence of Pertussis

Model	N	R	R Square	Adjusted R Square	Standard Error of the Estimate
	86	.252	.063	.052	19.08712

Table 12

ANOVA Data Associated with Adolescent Booster Schedule Type and Incidence of Pertussis

Model	Sum of Squares	df	Mean Squares	F	Sig
Regression	2069.147	1	2069.147	5.680	.019
Residual	30602.723	84	364.318		
Total	32671.870	85			

The F-Test, with a value of 5.680, indicates that the independent variables (required or recommended schedules) do have explanatory power over the dependent variable (booster incidence). The significance (P value) was .019, which is less than .05.

Table 13

Linear Regression Associated with Adolescent Booster Schedule Type and Incidence of Pertussis

Model	N	Coeff Std Error	t	sig	95% Conf Lower	95% Conf Upper
Required	86	4.126	2.383	.019	1.628	18.040

The value of t falls between the upper and lower confidence limits for both the recommended and required schedules. The t-value was 2.83, with a 95% lower confidence limit of 1.628 and a 95% upper confidence limit of 18.040. The coefficients had a positive relationship. The effect size was .252 indicating a small relationship. The significance (P value) was .019, which is less than .05, thus rejecting the null hypothesis.

Research Question 4

The data associated with Research Question 4 was analyzed utilizing European Center. The research question was:

> RQ 4: Is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles?

The linear combination of the addition of a required or recommended adolescent booster was not significantly related to pertussis epidemiologic cycles in the European countries evaluated as part of the doctoral study. The $R^2 = .001$, $F(1,84) = .120$, $p = .730$. coefficient of determination was .001. Therefore, the required or recommended adolescent boosters are not a good predictor of the pertussis epidemiologic cycles in the European countries evaluated as part of the doctoral study. The descriptive characteristics, linear regression model summary, ANOVA, and linear regression coefficients data are exhibited in Tables 14, 15, 16, and 17 below.

Table 14

Descriptive Characteristics Associated with Adolescent Booster Schedule Type and Length of Epidemiologic Cycles

Variable	N	Mean	Std Dev
Pertussis Booster Cycle	86	.4643	11.51829
Required schedule	86	.470	.502
Recommended schedule	86	.530	.502

The mean of the pertussis cycle was .4643. The mean of the recommended schedule data was larger than the mean of the required schedule data by .060.

Table 15

Linear Regression Associated with Adolescent Booster Schedule Type and Length of Epidemiologic Cycles

Model	N	R	R Square	Adjusted R Square	Standard Error of the Estimate
	86	.038	.001	-.010	11.57836

Table 16

ANOVA Associated with Adolescent Booster Schedule Type and Length of the Epidemiologic Cycles

Model	Sum of Squares	df	Mean Squares	F	Sig
Regression	16.503	1	16.121	.120	.730
Residual	11260.907	84	134.058		
Total	11277.028	85			

The F-Test, with a value of .120, indicates that the independent variables (required or recommended schedules) do not have explanatory power over the dependent variable (pertussis booster cycle). The significance (P value) was .730, which is greater than .05, thus not rejecting the null hypothesis.

Table 17

Linear Regression Associated with Adolescent Booster Schedule Type and Length of Epidemiologic Cycles

Model	N	Coeff Std Error	t	sig	95% Conf Lower	95% Conf Upper
Required	86	2.503	.347	.730	-4.110	5.846

The value of t falls between the upper and lower confidence limits for both the recommended and required schedules. The t-value was .347, with a 95% lower confidence limit of -4.110 and a 95% upper confidence limit of 5.846. The coefficients had a positive relationship. The effect size was .038 indicating a small relationship. The significance (P value) was .730, which is greater than .05, thus accepting the null hypothesis.

Summary

The study findings from Research Question 1 suggests that the pertussis immunization, whether recommended or required, does have an influence on the incidence rate of pertussis within the populations of European countries analyzed as part of this doctoral study. The same influence on pertussis incidence was demonstrated within the populations of European countries analyzed as part of this doctoral study related to the recommended or required adolescent boosters that were part of the pertussis immunization schedule. This influence was demonstrated through Research Question 3.

The doctoral study data also revealed via Research Question 2 that the pertussis immunization, recommended or required, does not have a relationship with the epidemiologic cycle of pertussis within the populations of European countries analyzed as part of the doctoral study. The same lack of relationship on the epidemiologic cycle of pertussis was demonstrated via Research Question 4 within the populations of European countries analyzed as part of this doctoral study related to recommended or required adolescent boosters as part of the pertussis immunization schedule.

The next section of this doctoral study examines the interpretation of the results of the Four research questions. Additionally, an overview of the study limitations, recommendations for future research, implications for professional practice, and social change are presented. Lastly, Section 4 provides a conclusion of the findings of this doctoral study.

Section 4: Application of Professional Practice and Implications for Social Change

Introduction

The purpose of this doctoral study was to establish if there is any relationship between the pertussis immunization schedule design (with and without the inclusion of adolescent boosters) and the immunization requirement (recommended or required), which potentially influences immunity waning and thus the incidence rate and epidemiologic cycles of pertussis within a country's population. Multiple European countries with recommended and mandatory pertussis immunization schedules were included in this study. The findings suggest that there is evidence of potential relationships associated between the immunization schedule and the immunization requirement on the incidence of pertussis. The same relationship was not observed between the epidemiologic cycles, the inclusion of adolescent boosters, and the incidence of pertussis.

Interpretation of Findings

The findings of this study via Research Questions 1 and 3 supported two of the research studies discussed in the section, Literature Review Related to Key Variables and/or Concepts, which mathematically modeled the effectiveness of acellular immunization strategies. Gambhir et al. (2015) utilized epidemiological modeling to examine the recent pertussis upsurge in the United States. The modeling identified variations in pertussis efficacy and immune protection duration of acellular vaccines. The results of the modeling pointed to the potential immune waning of acellular vaccines, and the fact that booster doses added to the immunization schedules may help reduce epidemics, thus lowering pertussis incidence (Gambhir, Clark, Cauchemez, Tartof, Swerdlow, & Ferguson, 2015).

The other mathematical modeling study was performed by Choi, Campbell, Amirthalingam, Jan van Hoek, and Miller (2016), who developed a mathematical model to examine the transmission of pertussis to understand the revival of pertussis in the countries of England and Wales. The results of the mathematical modeling indicated that the protection of the acellular vaccines did not appear as effective as the original whole-cell vaccine, thus creating an immune waning. The modeling predicted that if an adolescent booster were added to the immunization schedule, the pertussis incidence in infants could be lowered (Choi, Campbell, Amirthalingam, Jan van Hoek, & Miller, 2016).

The study evaluated the incidence and epidemiologic cycles of 15 European countries in relation to the required or recommended immunization schedule and required or recommended inclusion of an adolescent booster. The countries that met the established criteria were Austria, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Hungary, Ireland, Latvia, Lithuania, Norway, Portugal, Slovakia, Slovenia, and Sweden. The outcome of the linear regression analysis was interpreted by determining and assessing the linear regression equation, the coefficient of the multiple determination (R^2), the significance level, and the confidence intervals.

Research Question 1

The data associated with Research Question 1 were analyzed utilizing linear regression. The outcome of the linear regression analysis revealed that the null hypothesis, which was that no association between the pertussis vaccine schedule that is required or recommended by the European country and the incidence level of pertussis be rejected. The alternative hypothesis—that there was an association between the pertussis vaccine schedule that is required or recommended by the European country and the incidence level of pertussis—was supported by the results. Although there was not a strong linear relationship between the required or recommended immunization schedules and the incidence of pertussis, data analysis found that there was a significant relationship between the independent variable and the dependent variable.

The linear combination of required and recommended immunization schedules was found to be significantly related to pertussis incidence in the European countries evaluated as part of the doctoral study. The Coefficient of Determination was .056, indicating that approximately 5.6% of the variance in the dependent variable pertussis incidence in the population can be accounted for by the linear relationship of the independent variable of required and recommended immunization schedules. This relationship supports the work of Gambhir et al. (2015), whose study results indicated the need to perform more extensive modeling to examine alternative pertussis vaccination schedules, to aid in addressing the resurgence. This doctoral study confirmed a relationship between the schedule type and the incidence of pertussis, which also supported the Locht (2016) study results. Locht (2016) recommended that until more effective pertussis vaccines are developed, the optimal use of current vaccines is needed to control infection and prevent disease.

The theory of herd immunity suggests that infectious diseases that are contracted person to person are limited when a critical proportion of the population or the herd immunity threshold is protected through vaccination or natural immunity to the infectious disease, thus reducing the potential prevalence or resurgence of the disease in the population (Plans-Rubio, 2014). Although there was not a strong linear relationship between the required or recommended immunization schedules and the incidence of pertussis, the fact that there was a significant relationship between the independent variables of required or recommended immunization schedules and the dependent variable of the incidence of pertussis supports the theory of herd immunity by verifying the relationship between vaccination and incidence.

Research Question 2

The data associated with Research Question 2 were analyzed utilizing Linear regression. The outcome of the linear regression analysis revealed that the null hypothesis had no association between the pertussis vaccine schedule that is required or recommended by the European country and the epidemiologic cycles of pertussis, for Research Question 2 was supported by the results. The alternative hypothesis that there is an association between the pertussis vaccine schedule that is required or recommended by the European country and the epidemiologic cycles of pertussis was not supported by the results and was rejected. The data analysis found that there was not a significant relationship between the independent variable and the dependent variable.

The linear combination of required and recommended immunization schedules was not significantly related to pertussis epidemiologic cycles in the European countries evaluated as part of the doctoral study. The coefficient of determination was .001. Therefore, the required or recommended immunization schedules are not a good predictor of the pertussis epidemiologic cycles in the European countries evaluated as part of the doctoral study.

Although the required or recommended immunization schedules are not a good predictor of the pertussis epidemiologic cycles, the data obtained from this doctoral study does support findings from the research of Tan et al. (2015). Tan et al. (2015), suggested that the adolescent and adult populations are the most challenging to detect pertussis incidence due to the generalized characteristics and the lessened severity of pertussis in the adolescent and adult populations. The persistence of pertussis associated with the immune waning of the acellular vaccine in the adolescent and adult populations could account for the lack of relationship between the required or recommended immunization schedules and the epidemiologic cycles identified in this doctoral study.

The lack of a relationship between the required or recommended immunization schedules and the pertussis epidemiologic cycles could suggest a low-level persistence of pertussis in the population caused by the immune waning of the acellular vaccines. The lack of a relationship between the immunization schedule types and the pertussis epidemiologic cycles would also support the theory of herd immunity. If herd immunity in a population does not meet the required threshold, the herd effect will still provide a protective buffer of the population against the infectious disease (Holland & Chase, 2014).

Research Question 3

The data associated with Research Question 3 were analyzed utilizing linear regression. The outcome of the linear regression analysis revealed that the null hypothesis, that there is no association between the European country's addition of recommended adolescent boosters to the pertussis vaccine schedule and incidence level of pertussis, for Research Question 3 be rejected. The alternative hypothesis, that there was an association between the European country's addition of recommended adolescent boosters to the pertussis vaccine schedule and incidence level of pertussis, was supported by the results. Although there was not a strong linear relationship between the required or recommended immunization schedules and the incidence of pertussis, the data analysis found that there was a significant relationship between the independent variable and the dependent variable.

The linear combination of the addition of a required or recommended adolescent booster was found to be significantly related to pertussis incidence in the European countries evaluated as part of the doctoral study. The coefficient of determination was .063, indicating that approximately 6.3% of the variance of the dependent variable pertussis incidence in the population can be accounted for by the linear combination of the two independent variables of required and recommended adolescent boosters. The addition of an adolescent booster to the required or recommended immunization schedule has a stronger relationship to the incidence of pertussis than did the required or recommended immunization schedule without an adolescent booster. This finding supports the work of Gambhir et al. (2015), which concluded that there is a need for alternate vaccination schedules which would include adjustments to the age of vaccination, the age of booster doses, and cocooning strategies to help address the resurgence and persistence of pertussis. Additionally, the work of Radke et al. (2016) found that the vaccine protection from the immunization schedule only provides protection through age four. Further concluding that introducing a pertussis vaccine booster would enhance childhood immunity.

The primary objective of pertussis immunization programs is the reduction of disease and the associated mortality, and the potential establishment of population herd immunity (Nitsch-Osuch et al., 2013). The linear combination of the addition of a required or recommended adolescent booster was found to be significantly related to pertussis incidence in the European countries evaluated as part of the doctoral study. Additionally, the inclusions of an adolescent booster to immunization schedule type has a stronger relationship to the incidence of pertussis than did the immunization schedule type without an adolescent booster. These findings support the work of Osuch et al., (2013). Osuch et al., (2013) concluded in their research that the adherence to vaccination schedules and use of appropriately timed boosters, when immunity against pertussis waning is suspected, are essential to the establishment of herd immunity (Nitsch-Osuch et al. 2013). Osuch et al. (2013) further concluded in their research that the data provided evidence that European countries need to incorporate booster vaccinations into their immunization schedules to strengthen individual and population protection, and the establishment of strong herd immunity against pertussis infection and transmission (Nitsch-Osuch et al., 2013).

Research Question 4

The data associated with Research Question 4 were analyzed utilizing Linear regression. The outcome of the linear regression analysis revealed that the null hypothesis that there is no association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles for Research Question 4 was supported by the results. The alternative hypothesis that there is there any association between the European country's addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles, was not supported by the results and was rejected. The data analysis found that there was not a significant relationship between the independent variable and the dependent variable.

Although the addition of required adolescent boosters to the pertussis vaccine schedule and the length of the epidemiologic cycles did not show a relationship, the data obtained from this doctoral study do support findings from the research of Tan et al., (2015), as did the findings from Research Question 4. Tan et al. (2015) suggested that the adolescent and adult populations are the most challenging to detect pertussis incidence due to the generalized characteristics and the lessened severity of pertussis in the adolescent and adult populations. As stated in the findings for Research Question 2, the persistence of the pertussis associated with the immune waning of the acellular vaccine in the adolescent and adult populations could account for the lack of relationship between the required or recommended immunization schedules with the addition of adolescent boosters and the epidemiologic cycles identified in this doctoral study.

The lack of a relationship between the required or recommended immunization schedules and the pertussis epidemiologic cycles could suggest a low-level persistence of pertussis in the population caused by the immune waning of the acellular vaccines. The lack of a relationship between the immunization schedule types and the pertussis epidemiologic cycles would also support the theory of herd immunity. If herd immunity in a population does not meet the required threshold, the herd effect will still provide a protective buffer of the population against the infectious disease (Holland & Chase, 2014). However, it has been determined that the transmission of pertussis by adolescents and adults with waning pertussis immunity has caused the continuation of pertussis epidemiologic cycles in European countries (Heiniger et al., 2016).

Limitations of the Study

There were several limitations to the generalizability and validity of the data associated with the doctoral study. One of the limitations was that the data presented in the WVPDMSGS database for several of the European Union countries had missing data associated with the timeframe of interest from 2010 to 2017. Because several of the countries were missing a significant number of data points, the countries were not included in the study. Therefore, the study results were not reflective of all of the European Union countries. Additionally, the data associated with the data set utilized for this doctoral study are presumed to be accurate, but there are factors that could threaten the data accuracy. Although the data is evaluated for accuracy and reliability, the entry of the data into the database and the compilation of the data from the various reporting sources could be a potential threat to validity, if they were not performed per the WHO and UNICEF prescribed principles.

The validity of the data could also have been compromised if adequate reviews of the data were not performed by the WHO, UNICEF, local experts, and external reviewers. External validity threats also potentially exist associated with the WVPDMSGS database. External threats to the validity of the data being used to assess the research questions are the accuracy of the reporting and calculation of the immunization coverage from the participating member states. Additionally, biases could have been created if the participating member states failed to report portions of the population, or over or underestimated the vaccination coverage and incidence of the vaccine-preventable diseases.

Recommendations

The results of the study suggested that there is a connection between the immunization schedule and the timing and requirement for pertussis immunizations. Additional research is required to more thoroughly examine the timing based on the age of the immunization schedules. Additionally, the data from this doctoral study suggests that adolescent booster plays a role in contributing to the level of pertussis incidence in the European Union countries examined in this doctoral study. The addition of adolescent boosters to all pertussis immunization schedules, along with the timing and number of doses should be examined to determine the role that adolescent boosters contribute to the resurgence and persistence of pertussis.

Implications for Professional Practice and Social Change

The doctoral study results showed a relationship between immunization schedule types that were required or recommended on the incidence of pertussis. Furthermore, the immunization schedule types with the addition of an adolescent booster revealed a relationship associated with pertussis incidence rates. The data presented in this doctoral study also established a lack of a relationship with the immunization schedule type, required or recommended, and the design of the pertussis immunization schedule associated with epidemiologic cycles. The outcomes from this doctoral study, along with further research into the vaccination age and timing of the vaccinations associated with pertussis immunization schedules, could be applied in the field of public health to make significant improvements to pertussis immunization schedules to be used in the pertussis vaccination programs. The stated improvements to the pertussis immunization programs could reduce immune waning and, thus, lower the incidence of pertussis.

The data generated from this doctoral study provides physicians and government health agencies with an enhanced understanding of the relationship between the design and requirement of the immunization schedule on the incidence of pertussis and epidemiologic cycles. The data supports the need for the consideration of physicians and government health agencies regarding the implementation of required standardized immunization schedules, with the addition of an adolescent booster to the pertussis vaccination programs. The outcomes of this doctoral study also support the need to expand the research related to adolescent boosters and the role that they play in immune waning associated with acellular pertussis vaccines, along with the contribution that the immune waning has on the resurgence of pertussis.

This doctoral study assisted in providing relevant data that contributes to the knowledge base associated with some of the potential factors that may be causative to the resurgence and persistence of pertussis. This enhanced knowledge of the potential relationship between the addition of adolescent boosters and the requirement or recommendation of the immunization schedule on pertussis incidence could assist in controlling the pertussis resurgence, reduce immune waning through the use of adolescent boosters, enhance immunization schedule timing, and lower the incidence of pertussis resulting in positive social change through improved immunization programs and disease control strategies.

Conclusion

Pertussis is a vaccine-preventable disease, but the incidence of the disease continues to rebound in countries with high vaccination rates (Esposito & Principi, 2016). The use of vaccines is an essential tool to protect public health against pertussis. Not only do vaccines protect the immunized individual, but they also create a state of herd immunity that protects the population (Sabbe & Vandermeulen, 2016). Pertussis vaccines have played a protective role in reducing the incidence of pertussis. However, with the implementation of acellular vaccines, immunity is waning at a more rapid rate than with whole-cell vaccines (Sabbe & Vandermeulen, 2016).

The focus of this doctoral study was to gain an understanding of the potential relationship between the pertussis vaccination schedule, whether recommended, required, with an adolescent booster or without an adolescent booster, and the European country's pertussis incidence and epidemiologic cycles. The study findings suggest that the pertussis immunization, whether recommended or required, does have an influence on the incidence rate of pertussis within the populations of European countries analyzed as part of this doctoral study. The same influence on pertussis incidence was demonstrated related to recommended or required adolescent boosters as part of the pertussis immunization schedule.

The doctoral study data also revealed that the pertussis immunization, recommended or required, does not have a significant relationship with the epidemiologic cycle of pertussis within the populations of European countries analyzed as part of the doctoral study. The same lack of relationship on the epidemiologic cycle of pertussis was demonstrated related to recommended or required adolescent boosters as part of the pertussis immunization schedule.

This doctoral study assisted in providing relevant data that contributes to the understanding of the association with some of the potential factors that may be contributing to the resurgence and persistence of pertussis. Additionally, the data generated from this doctoral study provides an enhanced understanding of the relationship between the design and requirement of the immunization schedule on pertussis incidence. This enhanced understanding of the potential relationship between the design and requirement of the immunization schedule on pertussis incidence could assist in controlling the pertussis resurgence, reduce immune waning through the use of adolescent boosters, enhance immunization schedule timing, and lower the incidence of pertussis resulting in positive social change through improved immunization strategy.

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